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The effects of weather conditions on measles incidence in Guangzhou, Southern China

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Keywords: China, distributed lag non-linear model, effect, measles, weather condition

Abbreviations: MV, measles vaccine; EPI, Expanded Program on Immunization; DLNM, distributed lag non-linear model; SIA, supplement immunity activity; CI, confidence interval; Q-AIC, Akaike information criterion for quasi-Poisson; NS, natural cubic spline; RR, relative risk; Df, degree of freedom

Background: Few studies were conducted to examine the effects of weather conditions on the incidence of measles.

Methods: We used a distributed lag non-linear model (DLNM) to analyze the relationship between meteorological factors and measles incidence in Guangzhou, China.

Results: Nonlinear effects of temperature and relative humidity on measles incidence were observed. The relative risk (RR) for the measles incidence associated with the 75th percentile of mean temperature (27.9 °C) relative to the median of mean temperature (24.7 °C) was 1.00 (0.86,1.16) for lags 0–10 days. The RR for the measles incidence associated with the 25th percentile of relative humidity (64%) relative to the median of relative humidity (73%) was 1.36 (1.01,1.82) for lags 0–30 days. The wet effects and dry effects were larger in females than in males. The wet effects were generally increased with ages. Significantly negative effects of cold spells on measles incidence were observed.

Conclusion: Both hot and cold temperatures result in decreases in the incidence of measles, and low relative humidity is a risk factor of measles morbidity. An increased number of measles cases might occur before and after a cold spell. Our findings highlight the need to pay more attention to the weather transformation and improve the immunity of susceptible population for measles elimination. Catch-up vaccination campaigns should be initiated among young adults.

Introduction

Measles is a highly contagious disease caused by measles virus with a prodromal illness characterized by fever, fatigue, coryza, and cough before the onset of rash. Its complications include immune suppression after measles virus infection. Measles is primarily and easily transmitted by direct contact or droplet exposure, and humans are the only natural host. Measles contributed to millions of deaths annually worldwide before the introduction of the measles vaccines (MVs). However, there were still 454000 deaths resulting from measles following an intense international immunization campaign that has vaccinated over 200 million African children in 2004,[1] and measles caused an estimated 164000 deaths worldwide in 2008.[2] In recent years, many measles outbreaks occurred all over the world including China.[3-5]

In China, measles is categorized as a notifiable infectious disease with large numbers of measles cases reported in recent years. For example, in 2007 and 2008, there were 109023 and 131441 cases reported and the incidence rate were 8.29/100000 and 9.95/100000, respectively.[6,7]

The measles vaccine (MV) has been used in China since 1967. In 1986, the national Expanded Program on Immunization (EPI), providing a 2-dose monovalent MV schedule, was implemented in China, with the first dose of the vaccine being given at 8 mo of age (monovalent attenuated vaccine), and the second dose being given at 7 y of age (monovalent vaccine or measles-rubella/MR or measles-mumps-rubella/MMR vaccine).[8] Beginning in 2006, the second dose of MV has been administered at 18–24 mo of age, and all measles vaccinations are provided free of charge. The measles vaccination is usually performed by community health practitioners, and vaccination is mandatory for those aged from 8 mo to 14 y, including routine vaccination, follow-up Supplement Immunity Activities (SIAs), catch-up SIAs, and school-based vaccination.

In Guangzhou, the central city in Southern China, measles remains a public-health problem. After the implementation of the national EPI of a 2-dose monovalent measles vaccine

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schedule, the annual incidence rate of measles in Guangzhou was about 1.96 per 100000 population in recent years. However, the incidence rates have increased since 2004 (29.10, 22.33, 52.80, 32.08 per 100000 during 2004–2007).[9]

The morbidity of measles shows a seasonal variation. In temperate climates, measles outbreaks typically occur in the late winter and early spring every year, whereas in the tropics, measles outbreaks have irregular associations with rainy seasons,[10] which suggests that climatic factors partly underlie the seasonality of measles virus infections. Few studies are available on the effects of weather conditions on measles incidence regardless of frequent outbreaks of measles.

Guangzhou, a subtropical city in southern China, have experienced many extreme events in the context of global warming. Because of the warm weather and the weak ability to deal with climate change, people in this area are vulnerable to cold spells. For better estimations of the influence of climate change, it is necessary to explore whether there are impacts of cold spells on measles incidence in subtropical area.

In the current study, we used the time-series data for both monthly (2000–2012) and daily (2005–2008) measles cases to assess the effects of meteorological variables on the incidence of measles in Guangzhou, southern China by modeling lagged effects using distributed lag non-linear model (DLNM). We also explored the effects of cold spells on measles incidence. The findings of this study will provide insight into the relationships between weather variables and measles incidence and guide strategies and measures to help people protect themselves, especially the susceptible subpopulations.

Results

A total of 15625 measles cases were reported in Guangzhou during 2000–2012, whereas 76.5% (11,953) of the cases were reported (73.9% in people aged 0–14 y) from 2005 to 2008. The descriptive statistics for monthly/daily weather conditions and the monthly/daily incidence of measles are shown in **Table 1**. The average of monthly weather conditions during 2000–2012 were as follows: maximum temperature, 27.1 °C; mean temperature, 22.6 °C; minimum temperature, 19.4 °C; relative humidity, 73.4%; sunshine hours, 4.3 h, and air pressure, 1007.8 hPa. The average of daily weather conditions during 2005–2008 were close to the average of monthly weather conditions during 2000–2012.

According to the Spearman correlation analysis, the weather variables, except the monthly air pressure and the monthly relative humidity, were associated with the measles incidence. Because relative humidity has been proved to have an influence on occurrence and transmission of some viruses, we used the significant variables and relative humidity for the subsequent analyses.

For monthly cases, monthly mean temperature was associated with the lowest Q-AIC among the 3 temperature measures, whereas for daily cases, daily minimum temperature was associated with the lowest Q-AIC. Because the difference of Q-AICs between mean temperature and minimum temperature was small, and mean temperature provides easier and better interpretation of the results, we used mean temperature to conduct the DLNM.

Figure 1 shows the cumulative effects of the monthly/daily weather variables on the incidence of measles over the corresponding lag days. The relative risk of measles incidence increased before 18–20 °C but decreased afterwards. Relative humidity was inversely associated with the incidence of measles. There was a minor difference on the relationships between the monthly results and the daily results. In Guangzhou, the average of monthly sunshine hours had a negative relationship with the monthly incidence of measles below 5 h and had a positive relationship upper 5 h, whereas daily sunshine hours generally had a positive relationship with the daily incidence of measles.

Because the effects of monthly and daily sunshine hours are not exactly similar, and the daily meteorological data were more accurate than the monthly, we only calculated the estimate effects of daily comfortable mean temperature and relative humidity on the daily incidence of measles along the lags, with the 75th percentile of and the 25th percentile of the two meteorological variables to the median of themselves. The relative risk of the incidence of measles associated with the 75th percentile of mean temperature (27.9 °C) relative to the median of mean temperature (24.7 °C) was 1.00 (0.86, 1.16) for lags 0–10 d, and associated with the 25th percentile of mean temperature (18.5 °C) relative to the median of mean temperature (24.7 °C) was 0.78 (0.58, 1.06) for lags 0–10 d. The relative risk of the incidence of measles associated with the 75th percentile of relative humidity (81%) relative to the median of relative humidity (73%) was 0.92 (0.78, 1.08) for lags 0–30 d and associated with the 25th percentile of relative humidity (64%) relative to the median of relative humidity (73%) was 1.36 (1.01, 1.82) for lags 0–30 d.

Because the effect of daily relative humidity was apparently larger than the effect of daily mean temperature based on the results of **Figure 1**, and relative humidity can be obtained from the weather forecast or even be felt from our sense of comfortable, we calculated the effects of daily high (99th percentile) relative humidity (wet effects) and low (first percentile) relative humidity (dry effects) relative to the median of relative humidity during 2005 to 2008 (**Table 2**). The wet effects and dry effects were larger in females than in males. The wet effects were generally increased with ages, whereas the dry effects did not have a similar trend. The dry effects mostly influenced the subpopulation aged 1–14 y.

We hypothesized that cold spell occurrence is associated with the incidence of measles, and calculated the RRs comparing a non-cold spell period with the cold spell period. The measles reported cases were 26, 54 (24+30, January 11th to January 19th, and February 17th to February 26th), 72(30+42, January 4th to January 12th and February 24th to March 4th) during the case period, the first reference period and the second reference period, respectively. The RRs (95% confidence interval, CI) were 2.08 (1.30, 3.32) and 2.77 (1.77, 4.34) comparing the first reference period and the second reference period with the case period, respectively.

For daily data during 2005–2008, we changed df (4–7) for relative humidity and df (4–7) for sunshine hours and the

Table 1. Monthly/daily weather conditions and the monthly/daily incidence of measles in Guangzhou, southern China

Variable	Minimum	P25	Median	P75	Maximum	Mean	Std. deviation
	Monthly meteorological variables and monthly measles cases (2000–2012)						
Maximum temperature (°C)	14.0	22.1	28.1	32.0	34.9	27.1	5.5
Mean temperature (°C)	9.5	17.9	23.8	27.9	30.8	22.6	5.6
Minimum temperature (°C)	6.5	14.6	20.7	24.9	27.5	19.4	5.6
Relative humidity (%)	48.0	70.0	74.0	79.0	87.0	73.4	7.5
Duration of sunshine (h)	0.6	3.0	4.4	5.6	8.0	4.3	1.7
Air pressure (hPa)	994.3	1002.7	1008.0	1013.2	1018.9	1007.8	6.1
Number of measles cases	0	7	29	106	686	100	153.9
	Daily meteorological variables and daily measles cases (2005–2008)						
Maximum temperature (°C)	6.2	23.2	28.5	32.4	39.0	27.3	6.4
Mean temperature (°C)	5.4	18.5	24.7	27.9	34.2	22.9	6.3
Minimum temperature (°C)	2.1	15.2	21.6	25.1	30.4	19.9	6.3
Relative humidity (%)	20.0	63.5	73.0	81.0	95.0	71.1	13.4
Duration of sunshine (h)	0.0	0.0	3.4	7.3	11.4	3.9	3.5
Air pressure (hPa)	988.7	1003.2	1008.2	1014.1	1027.2	1008.6	6.9
Number of measles cases	0	3	6	12	40	8	6.8

maximum lag from 7–15 d for mean temperature, which gave similar results. When df (4–7 per year) for time to control for the season and long-term trends was given, the results were robust.

Discussion

In this study, we examined the effects of weather conditions on the incidence of measles in Guangzhou, southern China, and whether cold spell occurrence is associated with the incidence of measles was also explored. Our results indicated that there were nonlinear effects of the meteorological variables on the incidence of measles, except for air pressure. Both hot and cold temperatures resulted in decreases in the incidence of measles, and the most dangerous range of mean temperature was approximately 18 to 20 °C. Relative humidity was inversely associated with the incidence of measles. In Guangzhou, the average of monthly sunshine hours had a negative relationship with the monthly incidence of measles below 5 h and had a positive relationship upper 5 h, whereas daily sunshine hours generally had a positive relationship with the daily incidence of measles.

Although in China many national plans and measures are implemented to meet the World Health Organization's (WHO) goals for measles elimination, many measles outbreak occurred over the past few years. Few studies have explored the effects of weather conditions on the incidence of measles.[11] To our knowledge, this study is the first to examine the relationships between meteorological factors and the incidence of measles using a DLNM in China.

We observed that the effects of weather conditions on the measles incidence were nonlinear, except for air pressure. In our study, the relative risk of the measles incidence decreased with increased hot or cold temperature (upper or below 18–20 °C). Relative humidity was inversely associated with the incidence of measles. There are biological evidences to support the two findings. The virulence and survival of measles virus in air are mainly influenced by temperature and relative humidity. Measles virus is temperature-sensitive, and a study performed in laboratory shows that the survival of measles virus at 15 °C is slightly better than at 20 °C.[12] High temperature has influence on the survival of measles virus, and measles virus might survive a little better at low temperature while the activity of measles virus might decrease, which is totally consistent with our finding of the effect of mean temperature on the measles incidence. Studies also show that measles virus survival is remarkably dependent on relative humidity, and virus survives well at low relative humidity.[12,13] Therefore, with an increase in relative humidity, the incidence of measles decreases.

In our study, the relationship between the average of monthly sunshine hours and measles incidence is not exactly consistent with the relationship between daily sunshine hours and measles incidence. The main difference is the effects of sunshine hours below 5 h. We consider the reasons might be as follow: first, the monthly data included the data during 2000–2012, whereas the daily data were in 2005–2008, which is originally not the same. Second, measles virus is not strongly resistant to the external environment, and will be inactive half an hour in the sun,[14] which suggests that sunshine hours might be inversely associated with measles incidence. However, measles is a common childhood infections. Children aged 0–3 y usually stay at home and go to kindergarten or school after 4 y old. They spend more time indoor than outdoor in the daytime. Therefore, sunshine hours might not influence the incidence of measles too much, and the effects of sunshine hours we found might result from the relevancies of other meteorological factors and sunshine hours.

We found that the wet effects and dry effects were larger in females than in males, which might be explained by the

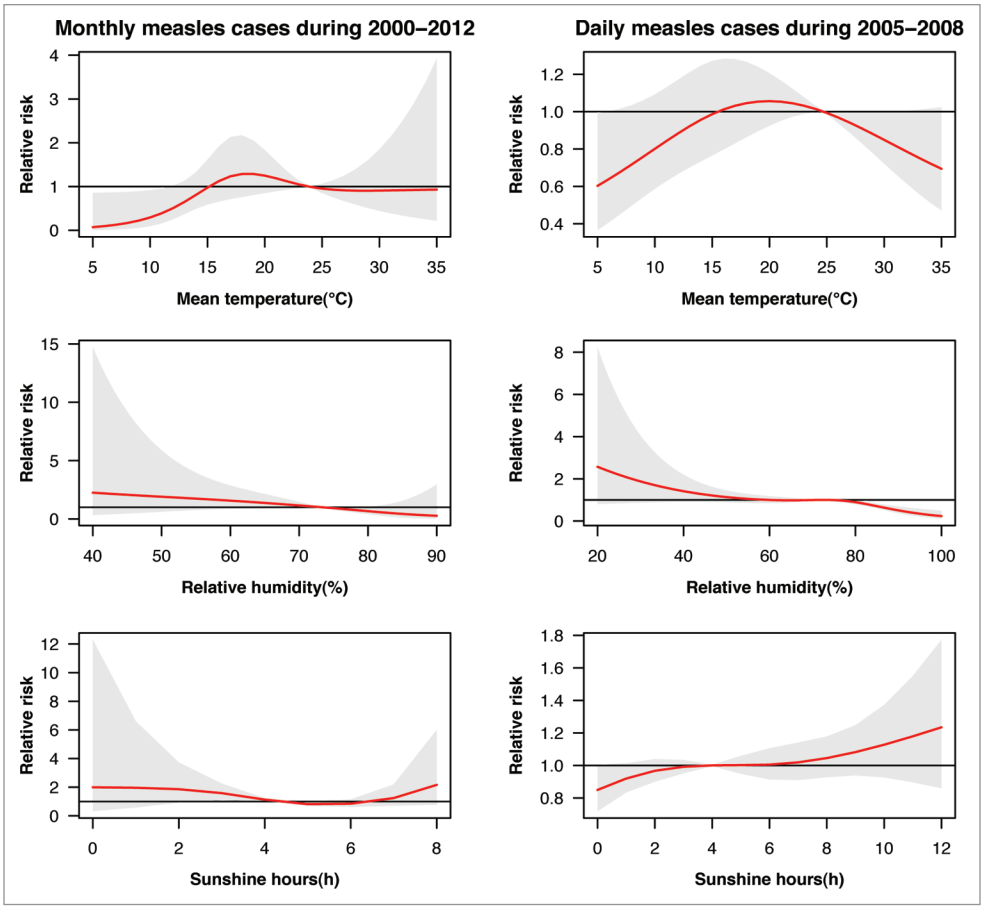

Figure 1. The estimated overall effects of the monthly/daily weather variables on the monthly/daily incidence of measles. For monthly cases, the lags of mean temperature, relative humidity, and sunshine hours are 2 mo. For daily cases, the lags of mean temperature, relative humidity, and sunshine hours are 30, 5, 10 d, respectively. The red lines represent mean relative risks, and gray regions represent 95%CIs.

differences of immune response, contacting frequency and time with susceptible population or confounding factors such as educational attainment, occupation between genders. Evidence suggests that measles mortality might be higher in girls than boys,[10] which might support the hypothesis of gender differences in physiology. A review indicates that physical activity shows a seasonal variation, being the highest in summer and the lowest in winter,[15] and the level of physical activity is generally higher in boys than girls,[16] which could result in the gender difference of wet effects and dry effects. Because measles virus is weak resistant to external environment, especially in the hot and sunny summer, and it is more crowded and poorer ventilated indoors than outdoors, boys who spend more time outdoors might be less risky to infections of measles virus than girls who usually spend more time indoors. In addition, mothers usually spend more time with their children than fathers, and thereby the risk of infections increases. The survival of measles virus is remarkably dependent on relative humidity. Therefore, the relative risk of measles incidence might mainly reflect in the effects of relative humidity.

The wet effects were generally increased with ages. We hypothesized this might be attributable to frequency of wet exposure and the antibody level of measles. In Guangzhou, high relative humidity often occurs in rainy days of summer, and children usually would not go out because of the bad weather and parents' forbiddance. Increased with age, an individual must go out and contact with more people for education, work or social activities. Moreover, a study in Guangzhou shows that people aged 15–29 y and women at childbearing age are the susceptible population because they are not currently advised to receive the measles vaccine vaccination in China.[9] However, we could not find a trend of dry effect by age similar to the wet effect, and the dry effect mostly influenced the subpopulation aged 1–14 y. The possible explanation is that people are equally exposed to dry days, and children aged 1–14 y are the targets of measles.

In the present study, we found that the effect of the cold spell on measles incidence was negative. We also found that the cases occurred at the part of the reference period afterward the case period are more than the cases occurred at the part of the reference period before the case period, although the difference is not significant. According to China Meteorological Administration, a cold spell results in a dramatic fall in temperature, strong wind, and rain and snow weather, which would decrease the incidence of measles based on the findings of our study. Cold exposure can cause physiological responses[17] and weaken the immune function,[18] which might increase the

Table 2. Relative risk of measles incidence associated with the wet and dry effects by gender and age

Variable	RR (95%CI)	
	Wet effect	Dry effect
Gender		
Male	**0.35 (0.20, 0.62)**	1.08 (0.50, 2.35)
Female	**0.50 (0.26, 0.96)**	**2.74 (1.15, 6.66)**
Age		
<1	**0.21 (0.11, 0.43)**	0.95 (0.33, 2.69)
1~14	**0.31 (0.15, 0.63)**	**3.17 (1.28, 7.88)**
>15	1.59 (0.71, 3.55)	1.05 (0.35, 3.17)

The wet effect was the relative risk of measles by comparing the 99th to the median of daily relative humidity. The dry effect was the relative risk of measles incidence by comparing the 1st to the median of daily relative humidity. The bold font means statistically significant.

risk of measles infection. Similar study indicates that a sharp rise or decrease in the environmental temperature related to the cold spell led to an increase of the SARS cases.[19] Our findings highlight the need to pay more attention to the weather transformation, especially strengthen the awareness of taking protective measures and avoiding close contact before and after a cold spell and improve the immunity of susceptible population. A reminding of preventive measures should be added to the weather forecast.

Although measles-containing vaccines are available, there are still many measles cases reported in Guangzhou. First, China has made great progress in the campaign for measles elimination, producing a continuous decline in the incidence of measles. However, the incidence of measles began to increase gradually after 2004, which may be due to the improved surveillance system in China since 2004. Second, transient population is the major target of the measles virus, China has undergone a remarkable period of rapid socio-economic development and urbanization. Guangzhou is a city with a large transient population, which accounting for nearly 40% of 12.6 million people; because of its rapid economic growth and relatively low cost of living, it has attracted a considerable portion of its population from other regions. With the exception of a small portion of the population with a high socio-economic status, including managers and technology personnel, the vast majority of the transient population works in manual labor, and many of these people emigrated from other places to avoid penalties from the local government for violating the one-child policy. In addition, the winter weather is moderate in Guangzhou and suitable for a transient population. Members of the transient population generally have a lower living standard, a lack of awareness regarding the vaccination needs of their children, and a tendency to neglect the mandatory vaccinations that are legally required for children in their resident regions. It has become a major challenge to eliminate measles in China.[20] Third, similar to other countries, infants in China are susceptible to measles infection due to insufficient antibodies prior to receiving the first dose of the vaccine within first year of life.[21]

In Guangzhou, the measles incidence of teenagers and adults has increased in recent years. During 2005–2008, 3120 of all notified measles cases (26.1%) were >14 y old. The similar situations that a shift in age distribution of measles cases toward older age groups were found even in some developed countries where measles has been controlled.[22,23] Nowadays people aged >14 y are not involved in the EPI program in China and few would like to receive the MV vaccination for measles prevention. Teenagers and young adults usually have low sero-positive prevalence, and have more social contacts than younger children, which results in the higher risk of measles.[24] Our findings also show that adults are more vulnerable to wet effects than youngers. Therefore, we recommend that catch-up vaccination campaigns should be promoted by using measles-containing vaccine (for example MMR or MR vaccine) among the young adults, who are not currently advised to receive the MV vaccination in China.

Several limitations should be mentioned. First, the findings of this study should be cautious to generalize to other areas because we only used data from one area. More studies with multiple cold spells or multi-city studies should be conducted to estimate the effect of cold spells. Second, the measles cases we used are mostly clinical diagnosed before 2006, which might overestimate the incidence. However, the clinical feature of measles is distinctive, so we believe that the overestimation will not be too much. Third, we did not control for wind speed and precipitation, because these data were not available.

To our knowledge, this study is the first to explore the effects of weather conditions and the incidence of measles using a DLNM in China. We used the monthly data during 2000–2012 and the daily data during 2005–2008 to construct models, respectively, and compared the 2 results to make our findings more reliable. We examined the wet and dry effects by gender and age to explore the susceptible populations and explored the effects of cold spells on the incidence of measles. Our findings proved that temperature and relative humidity have a significant effect on the incidence of measles, and an increase in daily incidence of measles occurred before and after the 2008 cold spell in Guangzhou. On the basis of findings in this study, decision makers from southern China, especially those have high measles incidence in their cities, must consider protective measures to protect vulnerable populations from weather transformations. Further study is needed to explore the effects of multiple cold spell and the effects of meteorological factors in multi-cities.

Materials and Methods

Guangzhou, located at 22°26′N to 23°56′N and 112°57′E to 114°3′E, is the largest metropolis in southern China with a population of over 12.75 million in 2012.[25] Influenced by the Asian monsoon, Guangzhou has a typical subtropical climate, in which summers are long, hot, and humid, and winters are short, mild, and dry.

Measles is a notifiable infectious disease in China and the monthly (2000–2012) and the daily (2005–2008) measles cases in Guangzhou were retrieved from Guangzhou Center for Disease Control and Prevention (GZCDC). The meteorological data during 2000–2012, including the daily maximum, mean, and minimum temperatures and relative humidity, air pressure, and sunshine hours, were obtained from China Meteorological Administration.

We performed the Spearman rank correlation tests to examine the relationship between monthly/daily measles incidence and the weather variables, and used the statistically significant variables to construct models. The monthly (2000–2012)/daily (2005–2008) measles incidence was modeled using a quasi-Poisson regression model combined with a DLNM. Proposed and developed in recent years, the DLNM is a flexible model that simultaneously estimates the nonlinearity and distributed lag effects of exposure-response relationship.[26,27] We used the Akaike information criterion for quasi-Poisson (Q-AIC) to choose the degree of freedom (df) for the meteorological variables and the df for their lags. For monthly cases, we used 2 df per year to control long-term trends and season. The effects of monthly temperature, relative humidity and sunshine hours were controlled for using 3 df natural cubic spline (NS) and 3df NS for lag up to 2 mo. For daily cases, we used 6 df per year to control long-term trends and season. The effects of daily temperature, relative humidity and sunshine hours were controlled for using 3 df NS and 3 df NS for lag up to 10, 30, and 5 d, respectively. We controlled for the day of the week and public holidays as categorical variables.

We fitted a model for each combination of temperature measures (the monthly/daily maximum, mean, and minimum temperature) and the incidence of measles and used the temperature with the lowest Q-AIC for the subsequent analyses. We conducted stratified analyses by gender and age group (<1, 1–14, >14years) to identify susceptible subpopulations to the effect of high or low relative humidity.

Extreme weather events, such as cold spells, frequently occur in recent years as a result of climate change. According to China Meteorological Administration, a cold spell in southern China was defined as a period with the temperature decreases at least 10 °C over 24 h or at least 12 °C over 48 h that results in the minimum temperature less than 5 °C. However, the definition is not suitable for Guangzhou, in which has a subtropical climate. Therefore, in this study, we defined a cold spell as ≥5 consecutive days with daily minimum temperature below the 5th percentile of temperatures recorded in Guangzhou from 1 January 2005 to 31 December 2008. This definition has been used in a previous study.[28] As a result, a cold spell was indentified between January 25 to February 9, 2008 in Guangzhou. We calculated the relative risks (RRs) comparing the cold spell period (case period) with a non-cold spell period (reference period) to determine whether cold spell occurrence is associated with the incidence of measles. We extended the case period by three subsequent days following the cold spell period for the possibility of lagged effects of cold spell. We selected the reference period as a bidirectional near-term winter reference period of the identical duration and with the identical distribution of the days of the week to minimize potential time-varying confounding effects. Therefore, the reference period could be 2 choices as follows: (1) January 11th to January 19th, 2008 and February 17th to February 26th, 2008; (2) January 4th to January 12th, 2008 and February 24th to March 4th, 2008.

All statistical tests were two-sided, and $P < 0.05$ was considered statistically significant. The analyses were performed using R software (version 3.0.2; R Development Core Team 2013) and the DLNM was constructed using the "dlnm" package.

Sensitivity analyses were performed for the daily data by changing the df (4–7 per year) for time to control for seasonality and secular trends, the df (4–7) for relative humidity, the df (4–7) for sunshine hours, and the maximum lag from 7–15 d for mean temperature. Study approval was obtained from the GZCDC ethics committee.

Disclosure of Potential Conflicts of Interest

No potential conflicts of interest were disclosed.

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